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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/637,190	08/11/2000	Mien-chie Hung	12005-002001	8780

26161 7590 12/03/2002

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BOSTON, MA 02110

EXAMINER
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CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/03/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
09/637,190

Applicant(s)  
Hung et al

Examiner  
Karen Canella

Art Unit  
1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 months MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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### **DETAILED ACTION**

1. Claims 1-20 are under consideration.
2. After consideration of applicants arguments and review and reconsideration of the instant claims, the finality of the Office action of Paper No. 9 is withdrawn.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### ***Claim Rejections Withdrawn***

4. The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Sager et al (USP 5,470,970) in view of Ding et al (Proceedings of the American Association of Cancer Research, 1996, Vol. 37, pp. A627) and either Gregory et al (USP 5,932,210) or Hung et al (USP 6,197,754) is withdrawn in light of applicants arguments.

#### ***New Grounds of Rejection***

5. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sager et al (USP 5,470,970) in view of the abstracts of Petrovich et al (Radiology, 1982, Vol. 144, pp. 905-908) and Weber et al (Otolaryngology-Head and Neck Surgery, 1988, Vol. 99, pp. 16-23) and Tytor et al (Clinical Otolaryngology, 1990, Vol. 15, pp. 235-252) and Eiband et al (American Journal of Surgery, 1989, Vol. 158, pp. 314-317) and Huwer et al (European Journal of Cardio-Thoracic Surgery, 1992, Vol. 6, pp. 498-502) and Nagel et al (Zentralblatt fur Chirurgie, 1994, Vol. 119, pp. 225-232) and van der Velden et al (Cancer, 1995, Vol. 75, pp. 2885-2890).

Claim 1 is drawn to a method of determining the probability of survival for a subject with squamous cell carcinoma, the method comprising determining the level of maspin gene expression in a biological sample and comparing said level with a threshold level, wherein a level of gene expression in the biological sample which is above the threshold level is indicative of a relatively high probability of survival. Claim 6 is drawn to a method of determining the probability of survival for a subject with squamous cell carcinoma, the method comprising determining the level of maspin gene expression in a biological sample and comparing said level with a threshold level,

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wherein a level of gene expression in the biological sample which is below the threshold level is indicative of a relatively low probability of survival. Claim 11 is drawn to a method of determining whether a subject with squamous cell carcinoma does not have a lymph node containing cancerous cells, the method comprising determining a level of maspin gene expression in a biological sample and comparing the level with a threshold level, wherein a level of maspin gene expression above the threshold level is indicative that the subject does not have a lymph node containing cancerous cells. Claim 16 is drawn to a method of determining whether a subject with squamous cell carcinoma does not have a lymph node containing cancerous cells, the method comprising determining a level of maspin gene expression in a biological sample and comparing the level with a threshold level, wherein a level of maspin gene expression below the threshold level is indicative that the subject has a lymph node containing cancerous cells. Claims 2, 7, 12 and 17 embody the methods of claims 1, 6, 11 and 16 respectively, wherein maspin gene expression is determined by measuring maspin protein. Claims 3, 8, 13 and 18 embody the methods of claims 2, 7, 12 and 17 respectively, wherein the amount of maspin protein is determined by an antibody that specifically binds to maspin. Claims 4, 9, 14 and 19 embody the methods of claims 1, 6, 11 and 16, respectively, wherein maspin gene expression is determined by measuring maspin mRNA. Claims 5, 10, 15 and 20 embody the methods of claims 4, 9, 14 and 19, respectively, wherein the level of maspin mRNA is determined by Northern Blot.

Sager et al teach a method for staging a carcinoma wherein the carcinoma is derived from cells which normally express the maspin gene, said method comprising the detection of maspin gene mRNA by northern blot. Wherein the amount of hybridization complex detected is less than about one-half, more preferably less than about one-third, and more preferably less than about one-tenth the amount found in the non-cancerous control cell is indicative that the test cell is cancerous and the absence of a hybridization complex with the mRNA of the test cell is indicative that the test cell is from an advanced, probably metastatic tumor, while an amount of hybridization complex that is detectable but substantially less, than in the control cell is an indication that the cell is from an early stage carcinoma that is probably not metastatic. Sager et al teach

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determination of the hybridization complex by Northern Blot (column 4, lines 24-57). Sager et al also teach the detection of the maspin protein by means of monoclonal or polyclonal antibodies , and the same correlation between the relative level of the immunocomplex in the test sample to the control sample (column 4, line 58 to column 5, line 15). Thus, Sager et al teaches the correlation between maspin gene expression in carcinomas and the relative likelihood of metastasis. Sager et al does not specifically teach a correlation between maspin levels and lymph node status, nor does Sager et al teach the probability of survival.

Petrovich et al and Weber et al and Tytor et al and Eiband et al and Huwer et al and Nagel et al and van der Velden et al all teach the correlation between metastasis to lymph nodes and poor survival in patients having squamous cell carcinoma.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to correlate the absence of a hybridization complex or an immunocomplex with metastasis to the lymph nodes and poor probability of survival; it would also have been obvious to correlate the decrease, (one-third less) of maspin gene expression with an early stage carcinoma that is probably not metastatic with relatively high probability of survival and a low probability of lymph node metastases. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Sager et al on the correlation between maspin gene expression and the likelihood of metastasis and the teachings of Petrovich et al and Weber et al and Tytor et al and Eiband et al and Huwer et al and Nagel et al and van der Velden et al on the correlation between the presence of lymph node metastases and poor survival in patients with squamous cell carcinoma.

### ***Conclusion***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

November 20, 2002

A handwritten signature in black ink, appearing to read 'Karen A. Canella', is located below the typed name. The signature is stylized and somewhat cursive.